IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:
Joel S. Echols, et al.	: Confirmation No. 1150
Appl. No.: 10/688,539	: Group Art Unit: 1615
Filed: October 17, 2003	: Examiner: Kishore, Gollamudi S.

For THREE LAYER ARTIFICAL TEAR FORMULATION

APPEAL BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S I R:

This is an appeal from the final rejection of claims 1-6 of the above-identified application.

I. REAL PARTY IN INTEREST

The real party in interest is Aqueous Pharma Limited, the assignee of record, as indicated by the assignment recorded on October 17, 2003 by the Assignment Division of the United States Patent and Trademark Office at Reel 014626, Frame 0275.

II. RELATED APPEALS AND INTERFERENCES

No other prior or pending appeals, interferences or judicial proceedings relating to, directly affecting or directly affected by this appeal, or having a bearing on the Board's decision in this appeal, are known to appellant, the appellant's legal representative, or assignee.

III. STATUS OF THE CLAIMS

Claims 1-6 are pending in the application. Claims 1-6 stand finally rejected by the Examiner as set forth in the Office Action dated January 22, 2008. Claims 7-21 have been cancelled. No claim stands withdrawn or allowed. The claims on appeal are claims 1-6 as they appear in the attached Claims Appendix.

IV. STATUS OF AMENDMENTS

On June 5, 2008, appellant filed one Amendment After Final subsequent to the final rejection made in the Office Action of January 22, 2008. This Amendment After Final was NOT entered by the Examiner as indicated in the Advisory Action Before the Filing of an Appeal Brief dated June 18, 2008.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Appellant's claimed invention relates in general to compositions for ophthalmic use, such as artificial tear formulations for the treatment of dry eye syndrome.

The subject matter of independent claim 1 is directed to a composition for ophthalmic use that comprises polyvinyl alcohol and polyvinyl acetate (see page 5, lines 5-19), a hydrophilic polymer (see page 5, lines 20-25), and a phospholipid (see page 5, line 26 through page 6, line 12).

The subject matter of claim 2 is directed to the composition of claim 1 wherein the phospholipid is formulated in polysorbate-80, glycerin, ethanol, and water (see page 5, line 28 through page 6, line 5).

The subject matter of claim 4 is directed to the composition of claim 1 further comprising water (see page 6, lines 4-5), one or more electrolytes to contribute to the well being of the corneal epithelium (see page 6, lines 13-16),

one or more preservatives (see page 6, lines 16-21), and one or more buffers (see page 6, lines 21-22).

The subject matter of claim 5 is directed to the composition of claim 1 wherein the hydrophilic polymer is polyvinyl pyrrolidone (see page 5, lines 22-23).

The subject matter of claim 6 is directed to the composition of claim 1 wherein the concentration of the polyvinyl alcohol is from about 0.5% to 10% by weight in water, the polyvinyl alcohol being about 96% to 99% hydrolyzed, and the concentration of the polyvinyl acetate is from about 0.5% to 10% by weight in water, the polyvinyl acetate being about 73% to 93% hydrolyzed (see page 5, lines 9-10 and lines 15-19). Claim 6 also recites that the concentration of the polyvinyl pyrrolidone is from about 0.5% to 10% by weight in water (see page 5, lines 23-25), and the concentration of the phospholipid is from about 0.003% to 0.02% by weight in water (see page 5, lines 26-27).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1-6 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention.

2. Claims 1-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,132,751 to Suzuki et al ("Suzuki et al") in combination with U.S. Patent No. 5,540,930 to Guy et al ("Guy et al") and U.S. Patent No. 4,883,658 to Holly ("Holly").

3. Claims 1-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,132,751 to Suzuki ("Suzuki") in combination with U.S. Patent No. 5,540,930 to Guy ("Guy") and U.S. Patent No. 4,883,658 to

Holly ("Holly"), and further in view of appellant's statements of prior art. (It is noted that in the Office Action of January 22, 2008 indicates that claims 1-7 are rejected on this ground of rejection. However, this appears to be a typographical error because claim 7 was previously cancelled.)

VII. ARGUMENT

1. Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-4 and 6

The Examiner states that the distinction between the hydrophilic polymer and the polyvinyl acetate and polyvinyl alcohol in claim 1 is unclear and that the claims do not recite polyvinyl acetate, polyvinyl alcohol and a hydrophilic polymer other than these two.

Appellant respectfully submits that one of ordinary skill in the art, when reading claim 1 in light of the specification, would understand that the recitation of "a hydrophilic polymer" in claim 1 would mean a hydrophilic polymer other than polyvinyl acetate and polyvinyl alcohol. As stated in MPEP 2173.02, the "test for definiteness under 35 U.S.C. 112, second paragraph, is whether 'those skilled in the art would understand what is claimed when the claim is read in light of the specification,'" *quoting Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). The present specification describes including both polyvinyl acetate and polyvinyl alcohol in the second paragraph on page 5, and mentions mixing polyvinyl acetate and polyvinyl alcohol to lower surface tension. In the next paragraph on page 5, the specification describes including a hydrophilic polymer to achieve a certain oncotic pressure. Thus, when claim 1 is read in light of the specification, one skilled in the art would recognize that the hydrophilic polymer recited in claim 1 is in addition to the polyvinyl acetate and polyvinyl alcohol. Appellant respectfully

submits that the language of claim 1 points out the subject matter with a reasonable degree of clarity and particularity.

For the above reasons, appellant respectfully submits that the rejection of claim 1, and the claims depending therefrom, under 35 U.S.C. § 112, second paragraph, is in error and should be reversed.

Claim 5

Claim 5 depends from claim 1 and is believed to be definite within the meaning of 35 U.S.C. § 112, second paragraph, for the reasons set forth above. Furthermore, claim 5 recites that the hydrophilic polymer of claim 1 is polyvinyl pyrrolidone. Thus, claim 5 removes any basis whatsoever for any confusion about the distinction between this hydrophilic polymer and polyvinyl acetate and polyvinyl alcohol. Accordingly, appellant respectfully submits that the rejection of claim 5 under 35 U.S.C. § 112, second paragraph, is in error and should be reversed.

2. Rejection under 35 U.S.C. § 103(a) over Suzuki et al in combination with Guy et al and Holly

Claims 1-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Suzuki et al in combination with Guy et al and Holly. Section 103(a) of the Patent Act states, in pertinent part, "[a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a).

The Supreme Court has set forth a framework for applying the statutory language of § 103 in *Graham v. John Deere Co. of Kansas City*, 383

U.S. 1, 148 USPQ 459 (1966). In *Graham*, the Court held that "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." *Graham,* 383 U.S., at 17, 148 USPQ, at 467.

The Supreme Court recently reiterated the *Graham* framework in *KSR International Co. v. Teleflex Inc.,* 550 U.S. ___, 82 USPQ2d 1385, 1391 (2007). While rejecting application of rigid and mandatory formulas in *KSR*, the Court states that " '[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.' " *KSR*, 550 U.S., at ____, 82 USPQ2d, at 1396 (quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). The Court further states that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art," (550 U.S., at ____, 82 USPQ2d, at 1396) and that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" (*Id.*).

For the reasons discussed below, appellant submits that claims 1-6 are not rendered unpatentable by the combination of Suzuki et al, Guy et al and Holly.

Claims 1, 3 and 5

Independent claim 1 recites a composition for ophthalmic use comprising polyvinyl alcohol, polyvinyl acetate, a hydrophilic polymer, and a phospholipid.

In contrast, Suzuki et al discloses an emulsion composition, the primary components of which are: 1) one drug selected from the group consisting of fluorometholone, clobetasone butyrate and clobetasol propionate, 2) a phospholipid, 3) liquid paraffin, and 4) water (see column 2, lines 5-14). In the last paragraph of column 6, Suzuki et al mentions other non-essential components that can be included in the emulsion. These additional components include thickeners such as polyvinyl pyrrolidone and polyvinyl alcohol, among others. Examples 16 and 23 describe using polyvinyl alcohol but not polyvinyl pyrrolidone. Examples 17 and 24 describe using polyvinyl pyrrolidone but not polyvinyl alcohol. Suzuki et al does not disclose using both polyvinyl pyrrolidone and polyvinyl alcohol together in the same composition. Thus, Suzuki et al describes a composition including a phospholipid and a hydrophilic polymer (i.e., polyvinyl pyrrolidone) and a composition including a phospholipid and polyvinyl alcohol, but Suzuki et al does not disclose a composition that includes the three components of a phospholipid, a hydrophilic polymer (polyvinyl pyrrolidone), and polyvinyl alcohol. The Examiner has not provided any reason as to why it would have been obvious to one of ordinary skill in the art to provide the composition of Suzuki et al with both polyvinyl alcohol and a hydrophilic polymer such as polyvinyl pyrrolidone with a phospholipid.

Another difference between Suzuki et al and claim 1 is that Suzuki et al does not disclose polyvinyl acetate. The Examiner contends that the "addition of polyvinyl acetate in Suzuki would have been obvious to one of ordinary skill in the art since the combination of polyvinyl acetate and polyvinyl alcohol is synergistic as taught by Holly." Holly does describe mixing polyvinyl acetate and polyvinyl alcohol to be "synergistic." Specifically, lines 25-29 in column 4 of Holly state that a mixture of polyvinyl acetate and polyvinyl alcohol was found to "lower the surface tension of the solution while forming a completely wettable adsorbed layer over hydrophobic solids." This formulation is disclosed

as being effective in treating tear film instability, as mentioned in the Abstract of Holly.

However, just because a mixture of two elements is taught to be "synergistic" does not mean that it would be obvious to combine these two elements in every composition that contains one of the two elements. Suzuki et al is concerned with increasing the solubility of drugs such as fluorometholone, clobetasone butyrate and clobetasol propionate so as to facilitate dispensing these drugs via aqueous eye drops. Suzuki et al is not concerned with tear film instability, which is the problem that the Holly patent is concerned with (see column 1) and addresses by proposing a synergistic mixture of polyvinyl acetate and polyvinyl alcohol. There is no suggestion that lowering surface tension by adding polyvinyl acetate to the polyvinyl alcohol already present in the Suzuki et al composition will improve the ability to dispense drugs such as fluorometholone, clobetasone butyrate and clobetasol propionate. Accordingly, one of ordinary skill in the art would not have been taught by Holly to add polyvinyl acetate to the compositions of Suzuki et al or Suzuki et al combined with Guy et al.

In the January 22, 2008 Office Action, the Examiner contends that this argument is not persuasive because the "instant claims are composition claims and motivation to use the combination need not be the same as applicant's." Appellant notes that no legal authority has been provided for this assertion, but submits that it is not applicable to appellant's argument in any event. Appellant is arguing that it would not have been obvious to modify the Suzuki et al reference with the teaching of the Holly reference because the reason that Holly discloses mixing polyvinyl acetate and polyvinyl alcohol (lower surface tension) would not motivate one of ordinary skill in the art to add polyvinyl acetate to the Suzuki et al composition. There is no suggestion why lowering surface tension in the Suzuki et al composition would provide any benefit to the

Suzuki et al composition. Appellant's motivation for combining the claimed elements has no bearing on this argument.

The Examiner also argues "one of ordinary skill in the art would benefit from the advantages taught by Holly in Suzuki since both are drawn to the eye treatment compositions." Appellant respectfully submits that this argument does not provide a convincing line of reasoning to establish the "rational underpinning" supporting the legal conclusion of obviousness required by *KSR*. As stated above, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art" *KSR*, 550 U.S., at ____, 82 USPQ2d, at 1396. The mere fact that the claimed elements are known to be independently used in eye treatment compositions would not have prompted a person of ordinary skill in the relevant field to combine the elements. While *KSR* requires a flexible approach instead of a rigid application of the so-called teaching, suggestion or motivation test, an obviousness analysis "must still be careful not to allow hindsight reconstruction of references to reach the claimed invention." *Innogenetics N.V. v. Abbott Laboratories,* 85 USPQ 1641, 1648, footnote 3 (Fed. Cir. 2008).

The Court in *KSR* stated that a "combination of familiar elements ... is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S., at ____, 82 USPQ2d, at 1395. Appellant respectfully submits that the composition of claim 1 does more than yield predictable results. Specifically, page 4, lines 16-18, describe that an artificial tear formulation having a polyvinyl alcohol, a polyvinyl acetate, a hydrophilic polymer and a phospholipid replicates all three layers of the normal human tear film. There is nothing in the prior art of record that would suggest that the claimed elements would predictably result in a composition that replicates the three layers of the normal human tear film. The fact that the claimed elements work "together in an unexpected and fruitful

manner" supports the conclusion that claimed invention "was not obvious to those skilled in the art." *Id.*

It is noted that Holly teaches a composition that includes polyvinyl alcohol, polyvinyl acetate and a hydrophilic polymer, but not a phospholipid. Although this is not the basis of the Examiner's rejection, appellant nonetheless submits that it would not have been obvious to one of ordinary skill in the art to modify Holly by including a phospholipid. As mentioned above, the mere fact that the claimed elements are known independently does not make their combination obvious, and the claimed combination of elements provides more than yield predictable results.

For all of the above reasons, appellant respectfully submits that the combination of Suzuki et al, Guy et al and Holly does not render independent claim 1 obvious. Claims 3 and 5 depend from claim 1 and are thus also believed to be unobvious. Appellant respectfully submits that the rejection of claims 1, 3 and 5 under 35 U.S.C. § 103(a) is in error and should be reversed.

Claim 2

Claim 2 recites that the phospholipid recited in claim 1 is formulated in polysorbate-80, glycerin, ethanol, and water. The combination of Suzuki et al, Guy et al and Holly fails to suggest using a phospholipid formulated in polysorbate-80, glycerin, ethanol, and water. The Examiner states that Guy et al discloses an eye formulation that includes glycerol and TWEEN 80, and to include a surfactant such as TWEEN 80 in the formulation of Suzuki et al would have been obvious because Guy et al teaches the use of a non-ionic surfactant such as TWEEN 80 in ophthalmic formulations. (It is noted that TWEEN 80 is a trademark for polysorbate-80.) However, this reasoning again relies on the invalid argument that a combination of independently known elements is obvious,

and disregards the holding in *KSR* that there must be some reason or "rational underpinning" to support a finding of obviousness.

The Examiner also contends that Suzuki et al discloses using solvents such as ethanol. Suzuki et al does describe using a solvent such as ethanol for preparing the emulsion, but as stated in lines 44-46 of column 7, the solvent is subsequently distilled off. Accordingly, the finished emulsion does not actually contain ethanol. Thus, the prior art references relied on by the Examiner do not suggest using a phospholipid formulated in polysorbate-80, glycerin, ethanol, and water.

Accordingly, appellant respectfully submits that the rejection of claim 2 under 35 U.S.C. § 103(a) is in error and should be reversed.

Claim 4

Claim 4 recites that the composition of claim 1 further includes water, one or more electrolytes to contribute to the well being of the corneal epithelium, one or more preservatives, and one or more buffers. There is no teaching or suggestion in the prior art of record of using one or more electrolytes that contribute to the well being of the corneal epithelium, and the Examiner has provided no indication at all as to why this claimed feature would have been obvious.

Accordingly, appellant respectfully submits that the rejection of claim 4 under 35 U.S.C. § 103(a) is in error and should be reversed.

Claim 6

Claim 6 recites that the concentration of the polyvinyl alcohol is from about 0.5% to 10% by weight in water, the polyvinyl alcohol being about 96% to 99% hydrolyzed; that the concentration of the polyvinyl acetate is from about 0.5% to 10% by weight in water, the polyvinyl acetate being about 73% to

93% hydrolyzed; that the concentration of the polyvinyl pyrrolidone is from about 0.5% to 10% by weight in water; and that the concentration of the phospholipid is from about 0.003% to 0.02% by weight in water.

The prior art clearly fails to teach or suggest these claimed concentration levels, and the Examiner has provided no reasoning supporting the position that these claimed concentration levels would have been obvious.

Accordingly, appellant respectfully submits that the rejection of claim 6 under 35 U.S.C. § 103(a) is in error and should be reversed.

3. Rejection under 35 U.S.C. § 103(a) over Suzuki et al in combination with Guy et al and Holly and further in view of appellant's statements of prior art

Claims 1-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Suzuki et al in combination with Guy et al and Holly and further in view of appellant's statements of prior art. As an initial point, appellant notes that the Examiner has rejected claim 1-6 as being obvious over *both* the combination of Suzuki et al, Guy et al and Holly *and* the combination of Suzuki et al, Guy et al, Holly and appellant's statements of prior art. It is not clear why the same claims that are alleged to be obvious over the combination of Suzuki et al, Guy et al and Holly only are also being rejected over the combination of Suzuki et al, Guy et al and Holly *plus* appellant's statements of prior art. Nevertheless, appellant submits that claims 1-6 are not rendered unpatentable by the combination of Suzuki et al, Guy et al and Holly and further in view of appellant's statements of prior art for the following reasons.

Claims 1-3 and 5

The Examiner argues that appellant's specification states "that the combination of lecithin, ethanol, glycerol, polysorbate 80 is readily available in the market under the trade name Amisol." However, just because a product is

commercially available does not mean that it would have been obvious to use that product in the claimed composition. Nothing in the prior art teaches using Amisol or a similar product as a source of a phospholipid in the claimed composition. As appellant has explained above, *KSR* holds that a patent claim is not shown to be obvious merely by demonstrating that each of its elements was independently known in the prior art. The mere fact that Amisol is a commercially available product does not make it obvious to use Amisol with the combination of Suzuki et al, Guy et al and Holly. There is simply no reason or "rational underpinning" that would have prompted a person of ordinary skill in the relevant field to combine Amisol with the combination of Suzuki et al, Guy et al and Holly.

For all of the above reasons, appellant respectfully submits that the combination of Suzuki et al, Guy et al, Holly and appellant's statements of prior art does not render independent claim 1 obvious. Claims 2, 3 and 5 depend from claim 1 and are thus also believed to be unobvious. Appellant respectfully submits that the rejection of claims 1-3 and 5 under 35 U.S.C. § 103(a) is in error and should be reversed.

Claim 4

As discussed above, the combination of Suzuki et al, Guy et al and Holly does not teach or suggest using one or more electrolytes that contribute to the well being of the corneal epithelium, as recited in claim 4. Appellant's statements of prior art also do not teach or suggest using one or more electrolytes that contribute to the well being of the corneal epithelium. Accordingly, appellant respectfully submits that the rejection of claim 4 under 35 U.S.C. § 103(a) is in error and should be reversed.

Claim 6

Similarly, the combination of Suzuki et al, Guy et al and Holly fails to teach or suggest the concentration levels recited in claim 6. Appellant's statements of prior art also do not teach or suggest these claimed concentration levels. Accordingly, appellant respectfully submits that the rejection of claim 6 under 35 U.S.C. § 103(a) is in error and should be reversed.

Conclusion

Appellant has shown the rejections under 35 U.S.C. 112, second paragraph, and 35 U.S.C. 103(a) to be in error. Therefore, the Board of Patent Appeals and Interferences is respectfully requested to reverse of the rejections of claims 1-6 and to hold all the claims to be allowable.

Respectfully submitted,

October 20, 2008
Date

/Patrick R. Scanlon/
Patrick R. Scanlon
Reg. No. 34,500
207-791-3110

VIII. CLAIMS APPENDIX

Claim 1. A composition for ophthalmic use, comprising:

a) polyvinyl alcohol;

b) polyvinyl acetate;

c) a hydrophilic polymer; and

d) a phospholipid.

Claim 2. The composition of claim 1 wherein said phospholipid is formulated in polysorbate-80, glycerin, ethanol, and water.

Claim 3. The composition of claim 1 wherein said phospholipid is lecithin.

Claim 4. The composition of claim 1 further comprising water, one or more electrolytes to contribute to the well being of the corneal epithelium, one or more preservatives, and one or more buffers.

Claim 5. The composition of claim 1 wherein said hydrophilic polymer is polyvinyl pyrrolidone.

Claim 6. The composition of claim 5 wherein the concentration of said polyvinyl alcohol is from about 0.5% to 10% by weight in water, said

polyvinyl alcohol being about 96% to 99% hydrolyzed; the concentration of said polyvinyl acetate is from about 0.5% to 10% by weight in water, said polyvinyl acetate being about 73% to 93% hydrolyzed; the concentration of said polyvinyl pyrrolidone is from about 0.5% to 10% by weight in water; and the concentration of said phospholipid is from about 0.003% to 0.02% by weight in water.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.